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NEWS 4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS 5	NOV 19	WPIX enhanced with XML display format
NEWS 6	NOV 30	ICSD reloaded with enhancements
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NEWS 10	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS 11	DEC 17	DGENE now includes more than 10 million sequences
NEWS 12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS 16	JAN 02	STN pricing information for 2008 now available
NEWS 17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS 18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS 19	JAN 28	MARPAT searching enhanced
NEWS 20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS 21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
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NEWS 24	FEB 20	PCI now available as a replacement to DPCI
NEWS 25	FEB 25	IFIREF reloaded with enhancements
NEWS 26	FEB 25	IMSPRODUCT reloaded with enhancements
NEWS 27	FEB 29	WPINDEX/WPIDS/WPIX enhanced with ECLA and current U.S. National Patent Classification

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NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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FILE 'HOME' ENTERED AT 18:33:02 ON 04 MAR 2008

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 18:33:11 ON 04 MAR 2008

 FILE LAST UPDATED: 4 Mar 2008 (20080304/UP).  FILE COVERS 1949 TO DATE.

  MEDLINE has been updated with the National Library of Medicine's
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  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s melanocortin-4
          2242 MELANOCORTIN
           395 MELANOCORTINS
          2341 MELANOCORTIN
                (MELANOCORTIN OR MELANOCORTINS)
       2572749 4
L1          516 MELANOCORTIN-4
                (MELANOCORTIN(W)4)

=> s l1 and MELANOCORTIN-4 receptor modulator
          2242 MELANOCORTIN
           395 MELANOCORTINS
          2341 MELANOCORTIN
                (MELANOCORTIN OR MELANOCORTINS)
       2572749 4
        605507 RECEPTOR
        628677 RECEPTORS
        843033 RECEPTOR
                (RECEPTOR OR RECEPTORS)
         13917 MODULATOR
         17840 MODULATORS
         30352 MODULATOR
                (MODULATOR OR MODULATORS)
             1 MELANOCORTIN-4 RECEPTOR MODULATOR
                (MELANOCORTIN(W)4(W)RECEPTOR(W)MODULATOR)
L2           1 L1 AND MELANOCORTIN-4 RECEPTOR MODULATOR

=> d ibib abs

L2   ANSWER 1 OF 1      MEDLINE on STN
ACCESSION NUMBER:    2007655875      MEDLINE  Full-text
DOCUMENT NUMBER:     PubMed ID: 17979771
```

TITLE: An integrated approach to fragment-based lead generation: philosophy, strategy and case studies from AstraZeneca's drug discovery programmes.

AUTHOR: Albert Jeffrey S; Blomberg Niklas; Breeze Alexander L; Brown Alastair J H; Burrows Jeremy N; Edwards Philip D; Folmer Rutger H A; Geschwindner Stefan; Griffen Ed J; Kenny Peter W; Nowak Thorsten; Olsson Lise-Lotte; Sanganee Hitesh; Shapiro Adam B

CORPORATE SOURCE: CNS Lead Generation Department, AstraZeneca R&D, 1800 Concord Pike, Wilmington, DE 19803, USA.. jeffrey.albert@astrazeneca.com

SOURCE: Current topics in medicinal chemistry, (2007) Vol. 7, No. 16, pp. 1600-29. Ref: 133
Journal code: 101119673. E-ISSN: 1873-4294.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200712

ENTRY DATE: Entered STN: 6 Nov 2007
Last Updated on STN: 19 Dec 2007
Entered Medline: 18 Dec 2007

AB Fragment-based lead generation (FBLG) has recently emerged as an alternative to traditional high throughput screening (HTS) to identify initial chemistry starting points for drug discovery programs. In comparison to HTS screening libraries, the screening sets for FBLG tend to contain orders of magnitude fewer compounds, and the compounds themselves are less structurally complex and have lower molecular weight. This report summarises the advent of FBLG within the industry and then describes the FBLG experience at AstraZeneca. We discuss (1) optimising the design of screening libraries, (2) hit detection methodologies, (3) evaluation of hit quality and use of ligand efficiency calculations, and (4) approaches to evolve fragment-based, low complexity hits towards drug-like leads. Furthermore, we exemplify our use of FBLG with case studies in the following drug discovery areas: antibacterial enzyme targets, GPCRs (melanocortin 4 receptor modulators), prostaglandin D2 synthase inhibitors, phosphatase inhibitors (protein tyrosine phosphotase 1B), and protease inhibitors (b-secretase).

```
=> s MELANOCORTIN-4 receptor
          2242 MELANOCORTIN
           395 MELANOCORTINS
          2341 MELANOCORTIN
                 (MELANOCORTIN OR MELANOCORTINS)
       2572749 4
        605507 RECEPTOR
        628677 RECEPTORS
        843033 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
L3         491 MELANOCORTIN-4 RECEPTOR
                 (MELANOCORTIN(W)4(W)RECEPTOR)

=> s l3 and (antagonist or agonist)
        135861 ANTAGONIST
        513596 ANTAGONISTS
        570363 ANTAGONIST
                 (ANTAGONIST OR ANTAGONISTS)
```

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        101616 AGONIST
        118175 AGONISTS
        172953 AGONIST
                  (AGONIST OR AGONISTS)
L4         266 L3 AND (ANTAGONIST OR AGONIST)

=> s l4 and cancer
        623819 CANCER
         90311 CANCERS
        650839 CANCER
                  (CANCER OR CANCERS)
L5           9 L4 AND CANCER

=> d ibib abs tot

L5   ANSWER 1 OF 9     MEDLINE on STN
ACCESSION NUMBER:    2007720315     IN-PROCESS  Full-text
DOCUMENT NUMBER:     PubMed ID: 17994683
TITLE:               Design, synthesis, in vitro, and in vivo characterization
                     of phenylpiperazines and pyridinylpiperazines as potent and
                     selective antagonists of the melanocortin
                     -4 receptor.
AUTHOR:              Tran Joe A; Jiang Wanlong; Tucci Fabio C; Fleck Beth A; Wen
                     Jenny; Sai Yang; Madan Ajay; Chen Ta Kung; Markison Stacy;
                     Foster Alan C; Hoare Sam R; Marks Daniel; Harman John; Chen
                     Caroline W; Arellano Melissa; Marinkovic Dragan; Bozigian
                     Haig; Saunders John; Chen Chen
CORPORATE SOURCE:    Department of Medicinal Chemistry, Neurocrine Biosciences,
                     Inc., 12790 El Camino Real, San Diego, California 92130,
                     USA.
SOURCE:              Journal of medicinal chemistry, (2007 Dec 13) Vol. 50, No.
                     25, pp. 6356-66.  Electronic Publication: 2007-11-10.
                     Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 11 Dec 2007
                     Last Updated on STN: 23 Jan 2008
AB   Benzylamine and pyridinemethylamine derivatives were synthesized and
     characterized as potent and selective antagonists of the melanocortin-4
     receptor (MC4R).  These compounds were also profiled in rodents for their
     pharmacokinetic properties.  Two compounds with diversified profiles in
     chemical structure, pharmacological activities, and pharmacokinetics, 10 and
     12b, showed efficacy in an established murine cachexia model.  For example,
     12b had a K(i) value of 3.4 nM at MC4R, was more than 200-fold selective over
     MC3R, and had a good pharmacokinetic profile in mice, including high brain
     penetration.  Moreover, 12b was able to stimulate food intake in the tumor-
     bearing mice and reverse their lean body mass loss.  Our results provided
     further evidence that a potent and selective MC4R antagonist with appropriate
     pharmacokinetic properties might potentially be useful for the treatment of
     cancer cachexia.


L5   ANSWER 2 OF 9     MEDLINE on STN
ACCESSION NUMBER:    2007369121     MEDLINE  Full-text
DOCUMENT NUMBER:     PubMed ID: 17584133
TITLE:               Melanocortin-4 receptor
                     antagonists as potential therapeutics in the
                     treatment of cachexia.
```

AUTHOR: Foster Alan C; Chen Chen
CORPORATE SOURCE: Neurocrine Biosciences Inc., San Diego, CA 92130, USA.. afoster@neurocrine.com
SOURCE: Current topics in medicinal chemistry, (2007) Vol. 7, No. 11, pp. 1131-6. Ref: 47
Journal code: 101119673. E-ISSN: 1873-4294.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200709
ENTRY DATE: Entered STN: 23 Jun 2007
Last Updated on STN: 25 Sep 2007
Entered Medline: 24 Sep 2007

AB The melanocortin-4 (MC4) receptor subtype plays a pivotal role in body weight regulation. Knock-out or mutation of MC4 receptors in animals or humans leads to severe obesity and acute or sub-acute antagonism of central MC4 receptors produces an increase in food intake and a decrease in metabolism. Knock-out or antagonism of MC4 receptors in animal models of cachexia leads to a protection from anorexia and the loss of both lean and fat body mass, suggesting that an MC4 antagonist may be beneficial in wasting diseases, which are poorly treated by available therapies. Considerable progress has been made in the discovery of non-peptide antagonists with high affinity and selectivity for MC4 receptors. Optimization of these compounds has produced molecules that are active upon systemic administration and are effective in protecting against cachectic symptoms in animal models of tumor-induced wasting. Further development of such compounds is greatly anticipated as a potential means to combat the cachexia that results from chronic diseases such as cancer, AIDS, renal failure, liver failure, congestive heart failure and lung disease.

L5 ANSWER 3 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2007349493 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17563464
TITLE: Melanocortin interventions in cachexia: how soon from bench to bedside?.
AUTHOR: DeBoer Mark D
CORPORATE SOURCE: Division of Endocrinology, University of Virginia, Charlottesville, Virginia 22908, USA.. mdd5z@virginia.edu
CONTRACT NUMBER: F32 DK072820-01A1 (United States NIDDK)
SOURCE: Current opinion in clinical nutrition and metabolic care, (2007 Jul) Vol. 10, No. 4, pp. 457-62. Ref: 66
Journal code: 9804399. ISSN: 1363-1950.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200710
ENTRY DATE: Entered STN: 13 Jun 2007
Last Updated on STN: 13 Oct 2007
Entered Medline: 12 Oct 2007

AB PURPOSE OF REVIEW: Cachexia is a condition of anorexia and wasting that accompanies many diseases including cancer, heart failure, and renal failure. One key center that is probably involved in the propagation of symptoms of cachexia is the melanocortin system in the hypothalamus and brainstem. This review focuses on cachexia treatment interventions that act via melanocortin

antagonism, by direct or indirect means. RECENT FINDINGS: Recent reports include a description of the physiology of the melanocortin system and its responsiveness to inflammatory cytokines. Regarding treatment potential, multiple reports describe the effectiveness of small molecule antagonists of the melanocortin-4 receptor in animal models of cachexia. These melanocortin antagonists, given by peripheral injection, improve food intake and lean body mass retention in the setting of cancer and renal failure. Additional reports provide evidence of melanocortin antagonism following treatment of cachexia using ghrelin and eicosonoic acid. SUMMARY: Cachexia is a serious condition that accompanies various disease states and currently does not have effective treatments. The melanocortin system may play a direct role in producing symptoms of cachexia, making antagonism of this system a logical objective for ameliorating these symptoms. Thus far, however, no data on human application have been published.

L5 ANSWER 4 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2006507711 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16932335
TITLE: Therapy insight: Use of melanocortin antagonists in the treatment of cachexia in chronic disease.
AUTHOR: DeBoer Mark D; Marks Daniel L
CORPORATE SOURCE: Department of Pediatrics, Oregon Health and Science University, Portland, OR 97239-2901, USA.
SOURCE: Nature clinical practice. Endocrinology & metabolism, (2006 Aug) Vol. 2, No. 8, pp. 459-66. Ref: 45
Journal code: 101261798. ISSN: 1745-8366.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200609
ENTRY DATE: Entered STN: 26 Aug 2006
Last Updated on STN: 22 Sep 2006
Entered Medline: 21 Sep 2006

AB Cachexia is a process that accompanies many chronic diseases, and consists of a combination of wasting of lean body mass, increased energy expenditure, and a paradoxical loss of appetite. Cachexia both worsens quality of life and negatively affects treatment of the underlying disease. Conditions as diverse as cancer, renal failure, and heart failure show a remarkable similarity in their associated cachexia, exhibiting changes in metabolism and endocrinology, including marked increases in levels of cytokines that accompany these diseases. So far, it has been difficult to treat disease-associated cachexia successfully. One treatment that has shown promise in animal trials, however, involves antagonism of the central melanocortin system, an anorexigenic pathway in the hypothalamus and brainstem. Humans who have genetic mutations involving pro-opiomelanocortin or the melanocortin 4 receptor in this pathway exhibit increased appetite and increased lean body mass. Recent research has shown that in rodent models of cancer and renal failure, administration of melanocortin 4 receptor antagonists results in an attenuation of symptoms of cachexia, including maintenance of appetite, lean body mass, and basal energy expenditure. Although this research needs to be substantiated in humans, it provides a promising direction for treating the wasting that is associated with a variety of disease states.

L5 ANSWER 5 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2006213166 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16436498

TITLE: Peripheral administration of a melanocortin 4-receptor inverse agonist prevents loss of lean body mass in tumor-bearing mice.
AUTHOR: Nicholson Janet R; Kohler Gotz; Schaerer Florian; Senn Claudia; Weyermann Philipp; Hofbauer Karl G
CORPORATE SOURCE: Applied Pharmacology, Biozentrum, University of Basel, Klingelbergstrasse 50, CH-4056 Basel, Switzerland.
SOURCE: The Journal of pharmacology and experimental therapeutics, (2006 May) Vol. 317, No. 2, pp. 771-7. Electronic Publication: 2006-01-25.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 19 Apr 2006
Last Updated on STN: 10 Jun 2006
Entered Medline: 9 Jun 2006

AB Cachexia affects many different chronically ill patient populations, including those with cancer. It results in loss of body weight, particularly of lean body mass (LBM), and is estimated to be responsible for over 20% of all cancer-related deaths. Currently, available drugs are ineffective, and new therapies are urgently needed. Melanocortin 4-receptor (MC4-R) blockade has been shown recently to be effective in preventing cancer cachexia in rodent models. In the present study, we have tested a MC4-R blocker, ML00253764 [2-{2-[2-(5-bromo-2-methoxyphenyl)-ethyl]-3- fluorophenyl}-4,5-dihydro-1H-imidazolium hydrochloride] (Vos et al., 2004), in vitro and in vivo. In membranes of human embryonic kidney 293 cells expressing human MC4-R, ML00253764 displaced [Nle(4), d-Phe(7)]-alpha-melanocyte-stimulating hormone binding with an IC(50) of 0.32 microM. At concentrations above 1 microM, ML00253764 decreased cAMP accumulation (maximal reduction of -20%) indicative of inverse agonist activity. ML00253764 was administered twice daily (15 mg/kg s.c.) for 13 days to C57BL6 mice bearing s.c. Lewis lung carcinoma tumors. Food intake and body weight were measured, and body composition was assessed using magnetic resonance relaxometry. ML00253764 stimulated light-phase food intake relative to vehicle-treated controls ($p < 0.05$), although no effect was observed on 24-h food intake. During the 21 days of the experiment, the LBM of tumor vehicle-treated mice decreased ($p < 0.05$). In contrast, the tumor-bearing mice treated with ML00253764 maintained their LBM. These data support the view that MC4-R blockade may be a suitable approach for the treatment of cancer cachexia and that MC4-R inverse agonists may have potential as drug candidates.

L5 ANSWER 6 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2005346575 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15919173
TITLE: Melanocortin-4 receptor in sheep: a potential site for therapeutic intervention in disease models.
AUTHOR: Sartin J L; Wagner C G; Marks D L; Daniel J A; McMahon C D; Obese F Y; Partridge C
CORPORATE SOURCE: Department Anatomy, Physiology & Pharmacology, Auburn University, AL 36849, USA.. sartijl@vetmed.auburn.edu
SOURCE: Domestic animal endocrinology, (2005 Aug) Vol. 29, No. 2, pp. 446-55. Electronic Publication: 2005-04-07. Ref: 54
Journal code: 8505191. ISSN: 0739-7240.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 7 Jul 2005
Last Updated on STN: 2 Sep 2005
Entered Medline: 1 Sep 2005

AB Reduced appetite combined with increased metabolic rate and decreased lean body mass is a major consequence of disease and other stressors. Studies in rodent species suggest that an understanding of appetite regulation may provide methodologies for intervention to prevent the deterioration of body mass such as observed with cancer or infectious diseases. For example, melanocortin-4 receptor (MC4-R) antagonists have shown a remarkable ability to reverse or prevent cachexia in rodents with sarcoma or treated with endotoxin. Studies in sheep have indicated that a number of peptide neurotransmitters may have a role in regulating appetite in this species. For example, agouti related protein mRNA and protein levels are dramatically altered with fasting in sheep. Moreover, agouti related protein, neuropeptide Y, melanin concentrating hormone and orexin are potent stimuli to increase feed intake in sheep. Recent studies have indicated that one of these neurotransmitters, NPY, can work in principal to improve appetite in endotoxin-treated sheep. Current studies are examining the role that MC4-R antagonists may have in the prevention or correction of body mass wasting diseases as well as practical applications in animal production.

L5 ANSWER 7 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2005256183 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15774557
TITLE: The regulation of feeding and metabolic rate and the prevention of murine cancer cachexia with a small-molecule melanocortin-4 receptor antagonist.
AUTHOR: Markison Stacy; Foster Alan C; Chen Chen; Brookhart Gregor B; Hesse Amy; Hoare Sam R J; Fleck Beth A; Brown Brock T; Marks Daniel L
CORPORATE SOURCE: Department of Pediatrics, Mailcode CDRCP, 707 Southwest Gaines Road, Portland, Oregon 97239, USA.. marksd@ohsu.edu
SOURCE: Endocrinology, (2005 Jun) Vol. 146, No. 6, pp. 2766-73. Electronic Publication: 2005-03-17.
Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 18 May 2005
Last Updated on STN: 29 Jun 2005
Entered Medline: 28 Jun 2005

AB Cachexia is metabolic disorder characterized by anorexia, an increased metabolic rate, and loss of lean body mass. It is a relatively common disorder, and is a pathological feature of diseases such as cancer , HIV infection, and renal failure. Recent studies have demonstrated that cachexia brought about by a variety of illnesses can be attenuated or reversed by blocking activation of the melanocortin 4 subtype receptor (MC4-R) within the central nervous system. Although the potential use of central MC4-R antagonists for the treatment of cachexia was supported by these studies, utility was limited by the need to deliver these agents intracerebroventricularly. In the current study, we present a series of experiments demonstrating that peripheral administration of a small molecule

MC4-R antagonist can effectively stimulate daytime (satiated) food intake as well as decrease basal metabolic rate in normal animals. Furthermore, this compound attenuated cachexia and preserved lean body mass in a murine cancer model. These data clearly demonstrate the potential of small molecule MC4-R antagonists in the treatment of cachexia and underscore the importance of melanocortin signaling in the development of this metabolic disorder.

L5 ANSWER 8 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2004302251 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15203150
TITLE: Synthesis and biological evaluation of imidazole-based small molecule antagonists of the melanocortin 4 receptor (MC4-R).
AUTHOR: Marsilje Thomas H; Roses Jonathan B; Calderwood Emily F; Stroud Stephen G; Forsyth Nancy E; Blackburn Christopher; Yowe David L; Miao Wenyan; Drabic Stacey V; Bohane Marie D; Scott Daniels J; Li Ping; Wu Lijun; Patane Michael A; Claiborne Christopher F
CORPORATE SOURCE: Department of Medicinal Chemistry, Millennium Pharmaceuticals, Inc., Cambridge, MA 02139, USA.. tmarsiljie@gnf.org
SOURCE: Bioorganic & medicinal chemistry letters, (2004 Jul 16) Vol. 14, No. 14, pp. 3721-5. Journal code: 9107377. ISSN: 0960-894X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 24 Jun 2004
Last Updated on STN: 8 Feb 2005
Entered Medline: 7 Feb 2005
AB A novel series of imidazole-based small molecule antagonists of the melanocortin 4 receptor (MC4-R) is reported. Members of this series have been identified, which exhibit sub-micromolar binding affinity for the MC4-R, functional potency <100nM, and good oral exposure in rat. Antagonists of the MC4-R are potentially useful in the therapeutic treatment of involuntary weight loss due to advanced age or disease (e.g. cancer or AIDS), an area of large, unmet medical need.

L5 ANSWER 9 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2003322627 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12851326
TITLE: Melanocortin signaling and anorexia in chronic disease states.
AUTHOR: Wisse Brent E; Schwartz Michael W; Cummings David E
CORPORATE SOURCE: Division of Metabolism, Endocrinology and Nutrition, Harborview Medical Center, University of Washington, Seattle, Washington 98104, USA.. beweisse@u.washington.edu
SOURCE: Annals of the New York Academy of Sciences, (2003 Jun) Vol. 994, pp. 275-81. Ref: 32 Journal code: 7506858. ISSN: 0077-8923.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 11 Jul 2003
Last Updated on STN: 30 Aug 2003
Entered Medline: 29 Aug 2003

AB Data from both rodent models and humans suggest that intact neuronal melanocortin signaling is essential to prevent obesity, as mutations that decrease the melanocortin signal within the brain induce hyperphagia and excess body fat accumulation. Melanocortins are also involved in the pathogenesis of disorders at the opposite end of the spectrum of energy homeostasis, the anorexia and weight loss associated with inflammatory and neoplastic disease processes. Studies using melanocortin antagonists (SHU9119 or agouti-related peptide) or genetic approaches (melanocortin-4 receptor null mice) suggest that intact melanocortin tone is required for anorexia and weight loss induced by injected lipopolysaccharide (an inflammatory gram-negative bacterial cell wall product) or by implantation of prostate or lung cancer cells. Although the precise mechanism whereby peripheral inflammatory/neoplastic factors activate the melanocortin system remains unknown, the proinflammatory cytokines (interleukin-1, interleukin-6, and tumor necrosis factor-alpha) that are produced in the hypothalamus of rodents during both inflammatory and neoplastic disease processes likely play a role. The data presented in this paper summarize findings that implicate neuronal melanocortin signaling in inflammatory anorexia.

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FILE 'MEDLINE' ENTERED AT 18:33:11 ON 04 MAR 2008
L1 516 S MELANOCORTIN-4
L2 1 S L1 AND MELANOCORTIN-4 RECEPTOR MODULATOR
L3 491 S MELANOCORTIN-4 RECEPTOR
L4 266 S L3 AND (ANTAGONIST OR AGONIST)
L5 9 S L4 AND CANCER

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